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USING ARTIFICIAL INTELLIGENCE IN LABORATORY DIAGNOSTICS FOR SEPSIS PATIENTS: SYSTEMATIC REVIEW OF ESR, CRP, AND MACHINE LEARNING PREDICTION MODELS

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Abstract

Background: Sepsis is a leading cause of morbidity and mortality, with existing diagnostic tools and biomarkers often proving insufficient for timely recognition. Recent advances in artificial intelligence (AI) and machine learning (ML) have shown potential to improve the early detection and prediction of sepsis using routinely available clinical and laboratory data. Methods: This systematic review was conducted according to PRISMA guidelines. A comprehensive search of PubMed, Scopus, Web of Science, and IEEE Xplore was performed for studies published between January 2017 and July 2025. Eligible studies applied AI or ML methods to predict sepsis or bacteremia in human populations using laboratory or electronic health record data and reported model performance metrics such as area under the receiver operating characteristic curve (AUC), sensitivity, or specificity. Data extraction and quality assessment using the Prediction Model Risk of Bias Assessment Tool (PROBAST) were conducted independently by two reviewers. Given the heterogeneity of study designs and outcomes, a narrative synthesis was performed. Results: Ten studies met the inclusion criteria, with diverse populations from neonates to critically ill adults and sample sizes ranging from 32 to over 366,000. Most models incorporated complete blood count (CBC), inflammatory biomarkers, or electronic health records, with methods including support vector machines, random forest, gradient boosting, and neural networks. Reported AUCs ranged from 0.79 to 0.99, with ML models generally outperforming conventional clinical scores such as SOFA and SIRS. Adult-focused studies consistently demonstrated strong predictive performance, while results in neonatal and pediatric populations were less robust. Despite promising results, several studies highlighted concerns regarding heterogeneity, limited external validation, and challenges with clinical integration. Conclusions: AI and ML

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models hold significant promise for improving the early detection and prediction of sepsis using routinely available data. These tools consistently outperform conventional diagnostic methods in adult populations, though evidence in neonates and children remains limited. Future research should prioritize multicenter prospective validation, standardization of predictor sets, and evaluation of real-world clinical impact to enable safe and effective implementation of AI-based decision support in sepsis care.

Keywords: Sepsis; Artificial Intelligence; Machine Learning; Early Detection; Prediction Models; Biomarkers; Electronic Health Records; Critical Care.

INTRODUCTION

Sepsis is a major global health burden, with estimated 50 million cases annually and more than 11 million deaths worldwide in 2017, representing 20% of all global mortality (van der Vegt et al. 2023). It is defined as a life-threatening organ dysfunction resulting from a dysregulated host response to infection and continues to be associated with high morbidity, mortality, and healthcare costs despite advances in intensive care (Islam et al. 2023).

Conventional prognostic and diagnostic tools, such as the Sequential Organ Failure Assessment (SOFA) and the Acute Physiology and Chronic Health Evaluation (APACHE) scores, have been widely used in critical care. However, these scores demonstrate limited calibration and predictive accuracy in contemporary sepsis populations, largely due to their reliance on linear models and inability to account for complex interactions among clinical variables (Musat et al. 2024). Similarly, biomarkers such as C-reactive protein (CRP), procalcitonin (PCT), and lactate, while commonly used, have restricted sensitivity and specificity when applied in isolation, limiting their utility for early diagnosis and prognosis (Lien et al. 2022).

Recent advances in artificial intelligence (AI) and machine learning (ML) have introduced new opportunities to overcome these limitations. By leveraging high-dimensional data derived from electronic health records (EHRs), laboratory results, and physiological parameters, ML algorithms can capture nonlinear patterns and temporal dynamics of sepsis that traditional approaches cannot (Islam et al. 2023). Systematic reviews of deployed sepsis prediction models have demonstrated that AI-based algorithms often outperform rule-based systems, achieving higher sensitivity, specificity, and area under the receiver operating characteristic curve (AUROC) values across diverse settings (van der Vegt et al. 2023; Musat et al. 2024). For example, models developed using complete blood count (CBC) and differential leukocyte count (DC) have reached AUROC values above 0.80, performing comparably or even superiorly to CRP- and PCT-based approaches (Lien et al. 2022).

Nevertheless, despite their potential, real-world adoption of AI models for sepsis remains limited. Many existing models are developed retrospectively on single-center datasets, with sparse external validation, which raises concerns about their generalizability and reliability across patient populations (Wang et al. 2025). Furthermore, practical challenges such as workflow integration, interpretability of complex models, and clinician trust continue to hinder successful implementation (van der Vegt et al. 2023).

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A recent methodological systematic review of real-time sepsis prediction algorithms highlighted that model performance often declines substantially when externally validated, underscoring the urgent need for prospective multicenter validation studies (Wang et al. 2025). This systematic review aims to evaluate the application of AI models for early detection and prognosis of sepsis, with a specific focus on those incorporating routinely available laboratory and clinical data. By critically appraising methodological rigor, predictive performance, and translational readiness, this review seeks to clarify the role of AI in sepsis care and identify priorities for future research and implementation.

METHODOLOGY

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, following a protocol that was developed prior to commencing the study. The protocol outlined the research objectives, inclusion and exclusion criteria, and the analytic framework.

The eligibility criteria were defined to ensure that only relevant studies were included. Original research articles that applied artificial intelligence (AI) or machine learning (ML) techniques to predict, diagnose, or stratify sepsis or bacteremia in human populations were considered. Studies were required to use routinely collected clinical or laboratory data such as complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), procalcitonin (PCT), vital signs, or electronic health records (EHRs). In addition, eligible studies needed to report at least one performance outcome measure, including the area under the receiver operating characteristic curve (AUC), sensitivity, specificity, or accuracy. Studies were excluded if they relied solely on rule-based algorithms, did not focus on sepsis prediction, or were published as conference abstracts without full-text availability. Non-English language articles and review articles were also excluded.

A comprehensive literature search was carried out across PubMed, Scopus, Web of Science, and IEEE Xplore to identify articles published between January 2017 and July 2025. The search strategy combined keywords and Medical Subject Headings (MeSH), including terms such as “sepsis,” “bacteremia,” “machine learning,” “artificial intelligence,” “prediction,” “electronic health record,” “C-reactive protein,” “procalcitonin,” and “complete blood count.” To ensure completeness, the reference lists of all included studies and relevant systematic reviews were also manually screened to identify additional eligible publications.

The study selection process involved two stages: title and abstract screening, followed by full-text review. All identified records were imported into Covidence software, where duplicates were removed. Two independent reviewers then assessed each record against the predefined eligibility criteria. Discrepancies were resolved through discussion until consensus was reached. The entire process was documented using a PRISMA flow diagram, which outlined the number of records identified, screened, excluded, and included in the final analysis.

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Data extraction was performed independently by two reviewers using a standardized template to ensure consistency. Extracted data included the citation details, year of publication, study design, sample size, population characteristics, clinical setting, predictors and tests used, AI or ML methods applied, and reported outcomes such as AUC, sensitivity, specificity, or other performance measures. The data were then organized into two comprehensive tables: one summarizing study design, sample size, predictors, and outcomes, and another focusing on demographic characteristics, tests performed, and main findings. To evaluate the methodological rigor of the included studies, the Prediction Model Risk of Bias Assessment Tool (PROBAST) was applied. Each study was assessed for potential bias across four domains: participant selection, predictor definition and measurement, outcome definition, and statistical analysis. Ratings of low, high, or unclear risk of bias were assigned, and disagreements were resolved through consensus. A narrative synthesis approach was adopted, allowing the integration of results across different studies. This method enabled the identification of common themes, strengths, and limitations in the existing literature.

RESULTS

A total of ten studies were included in this review, encompassing diverse populations ranging from neonates and pediatric surgical patients to adults in intensive care units and emergency departments. The included studies employed a variety of study designs, including prospective randomized trials, translational studies, retrospective analyses, and multicenter validations, with sample sizes ranging from 32 to over 366,000 participants. Collectively, these studies evaluated the role of artificial intelligence (AI) and machine learning (ML) approaches in the early prediction, diagnosis, and stratification of sepsis and bacteremia using routinely available laboratory tests, inflammatory biomarkers, electronic health records, and cell population data.

Across the studies, complete blood count (CBC) and erythrocyte sedimentation rate (ESR) emerged as consistent parameters in model development. Yesil et al. (2025) demonstrated that an SVM model achieved an AUC of 90.6% for sepsis prediction using CBC and ESR, although performance was modestly affected by analytical bias. Similarly, Padoan et al. (2025) reported that ESR kinetics could be effectively analyzed using machine learning, with gradient boosting models achieving an AUC of 0.800 and logistic regression validation yielding an AUC as high as 0.991 for sepsis detection. In another validation study, Persson et al. (2024) confirmed the prognostic accuracy of the NAVOY® Sepsis algorithm in the ICU, which identified sepsis three hours prior to onset with accuracy of 0.79, sensitivity of 0.80, and specificity of 0.78. Large-scale retrospective analyses provided additional support for the integration of AI with routine laboratory testing. Gunčar et al. (2024), using over 44,000 cases, developed an XGBoost model combining CBC and CRP values that achieved an AUC of 0.905, outperforming CRP-based decision rules. Lien et al. (2022), analyzing over 366,000 blood cultures, found that random forest models using CBC and differential leukocyte counts (DC) achieved an AUC of 0.802, which was superior to CRP or PCT alone, underscoring the predictive value of readily available hematological data. Chang et al. (2023) further expanded on this concept

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by integrating cell population data (CPD) with CBC and DC in over 20,000 patients, showing excellent predictive performance for bacteremia with AUCs between 0.812 and 0.847 across internal and external validation cohorts. The role of combined biomarker and clinical data was also highlighted in two studies. Taneja et al. (2017) demonstrated that a combination of six biomarkers (including IL-6, PCT, and G-CSF) with EMR data improved early sepsis identification, with combined models achieving an AUC of 0.81 compared to 0.75 for EMR alone. Choi et al. (2020) introduced a complementary model based on hematological parameters, which achieved superior predictive power (AUC 0.86) compared to traditional clinical scores such as SIRS, SOFA, or LODS.

Special populations were evaluated in two additional studies. Cabral et al. (2025) investigated a Bayesian model in 32 pediatric post-cardiac surgery patients, finding that the combination of sTREM-1, CRP, and leukocyte counts reliably predicted sepsis, with sTREM-1 alone yielding an AUC of 0.761. Conversely, Matsushita et al. (2023) reported that ML models based on CBC and CRP were not effective in predicting positive blood cultures among neonates in a NICU, with low predictive performance (F1-score 0.14–0.43), suggesting that neonatal populations may require alternative approaches or additional biomarkers. The findings show that AI models leveraging routine laboratory and clinical data can achieve high accuracy in sepsis prediction across diverse populations. While adult populations benefited from robust and generalizable models, evidence in neonates and pediatric patients remains limited and heterogeneous. These results highlight the promise of AI-driven diagnostic tools while also underscoring the need for population-specific validation and integration into clinical workflows.

Table 1: AI and Sepsis Prediction

Citation	Study design	Sample size	Population characteristics	Method	Outcome
Yesil et al., 2025	Model development and validation	n=211 (104 controls, 107 sepsis/acute inflammatory patients)	Outpatients and acute inflammatory status ward patients	Support Vector Machine (SVM) using CBC and ESR with bias simulations	AUC up to 90.6%; bias affected performance but no significant differences
Padoan et al., 2025	Comparative analysis and ML validation	346 samples (control, rheumatological, oncological, sepsis groups)	Patients with different inflammatory conditions	Gradient Boosting, SVM, Naïve Bayes, Neural Networks, Logistic Regression on ESR kinetics	Best AUC 0.800 (GBM); Logistic regression validation AUC 0.991 for sepsis detection
Persson et al., 2024	Prospective randomized controlled trial	304 ICU patients	Adult ICU patients at Skåne University	NAVOY® Sepsis algorithm with vital signs,	Predicted sepsis 3h before onset with accuracy 0.79, sensitivity

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			Hospital, including COVID-19 cases	labs, and blood gases	0.80, specificity 0.78
Gunčar et al., 2024	Retrospective ML model development	44,120 cases (UMC Ljubljana)	Adult, non-pregnant patients with viral or bacterial infections	XGBoost with CBC, CRP, sex, age	Accuracy 82.2%, AUC 0.905; outperformed CRP-only decision rule
Lien et al., 2022	Retrospective analysis	366,586 blood culture results (Taiwan)	Adult hospitalized patients	Logistic regression and random forest using CBC/DC ± CRP or PCT	Random forest AUC 0.802 with CBC/DC; similar or superior to CRP/PCT
Taneja et al., 2017	Retrospective model development	Large hospital cohort (exact n not specified in abstract)	Patients with sepsis and non-sepsis EMR data	ML combining 6 biomarkers (IL-6, nCD64, IL-1ra, PCT, MCP1, G-CSF) with EMR data	Biomarkers+EMR AUC 0.81 vs EMR alone AUC 0.75; improved early identification
Choi et al., 2020	Retrospective comparative analysis	Patients with sepsis vs fever (n not specified in abstract)	Fever patients compared with confirmed sepsis cases	Stepwise selection and ML combining hematological parameters	Complementary model AUC 0.86 vs 0.51–0.74 for traditional scores (SIRS, SOFA, LODS)
Chang et al., 2023	Prospective and external validation study	20,636 (derivation), 3,143 (prospective), 664 + 1,622 (external validation)	Adult ED patients with suspected bacterial infections	CatBoost ML model using CBC, differential count, and cell population data (CPD)	AUC 0.844 (derivation), 0.812 (prospective), 0.844–0.847 (external validation)
Cabral et al., 2025	Translational study	32 children with congenital heart disease post-surgery	Pediatric post-cardiac surgery patients	Bayesian network combining sTREM-1, CRP, and leukogram	Model predicted sepsis with 100% probability when thresholds exceeded; sTREM-1 AUC 0.761
Matsushita et al., 2023	Retrospective single-center NICU study	1181 blood cultures with CBC+CRP; 1911 with CBC only	Neonates in NICU, São Paulo, Brazil	ML models with CBC ± CRP	Low predictive power (F1 0.14–0.43, accuracy 0.688–0.864); not suitable for sepsis prediction

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Table 2: Demographics, Tests Performed, and Main Findings of AI Studies on Sepsis

Citation	Demographics	Tests performed	Main findings
Yesil et al., 2025	211 patients (104 controls, 107 sepsis/acute inflammation); outpatient + hospital ward	CBC, ESR with analytical bias simulations	SVM AUC 90.6%; analytical bias influenced results but not significantly
Padoan et al., 2025	346 samples from control, rheumatology, oncology, and sepsis patients	ESR by automated analyzers vs Westergren; ESR kinetics	ML (GBM best AUC 0.800); Logistic regression validation AUC 0.991 for sepsis
Persson et al., 2024	304 adult ICU patients (Skåne Univ. Hospital, incl. COVID-19 cases)	Routinely collected vitals, blood gases, lab values	NAVOY® Sepsis predicted sepsis 3h before onset (accuracy 0.79, sens. 0.80, spec. 0.78)
Gunčar et al., 2024	44,120 adult, non-pregnant patients (viral or bacterial infections)	CBC, CRP, age, sex	XGBoost accuracy 82.2%, AUC 0.905; better than CRP alone
Lien et al., 2022	366,586 blood cultures from adult hospitalized patients (Taiwan)	CBC/DC, CRP, PCT	Random forest AUC 0.802 with CBC/DC; similar to or better than CRP/PCT
Taneja et al., 2017	Hospital cohort; sepsis and non-sepsis patients	6 biomarkers (IL-6, nCD64, IL-1ra, PCT, MCP1, G-CSF) + EMR data	Biomarkers+EMR AUC 0.81; biomarkers alone ~AUC 0.80; EMR alone 0.75
Choi et al., 2020	Fever patient's vs confirmed sepsis cases	Hematological parameters (WBC, platelets, bilirubin, creatinine, etc.)	Complementary model AUC 0.86 vs 0.51–0.74 for SIRS, SOFA, LODS scores
Chang et al., 2023	20,636 derivations; 3,143 prospective; 664+1,622 external validation (Taiwan hospitals)	CBC, differential count, CPD	CatBoost model AUC 0.844 derivation, 0.812 prospective, 0.844–0.847 external validation
Cabral et al., 2025	32 pediatric post-cardiac surgery patients (Brazil)	CRP, leukogram, sTREM-1	Bayesian model reached 100% probability when CRP>71, WBC>14k, sTREM-1>283 pg/mL
Matsushita et al., 2023	Neonates, NICU São Paulo, Brazil; 1181 CBC+CRP, 1911 CBC only	CBC, CRP	Low predictive power (F1 0.14–0.43, accuracy 0.688–0.864); not useful for sepsis prediction

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DISCUSSION

This systematic review synthesized evidence from ten studies evaluating the role of artificial intelligence (AI) and machine learning (ML) in the early detection and prediction of sepsis across diverse patient populations and clinical settings. Collectively, the findings support the potential of ML-driven approaches to outperform traditional scoring systems, although challenges related to heterogeneity, validation, and clinical integration remain.

One consistent observation across studies is the superior diagnostic accuracy of ML models compared to conventional methods. Fleuren et al. (2020) demonstrated that supervised ML models achieved AUROCs ranging from 0.68 to 0.99 in intensive care settings, with several models predicting sepsis onset well in advance of clinical recognition. Similarly, Moor et al. (2021) highlighted the ability of digital biomarker discovery using ML to refine early prediction, though they stressed significant inter-study heterogeneity and limited reproducibility. Subsequent reviews reinforced these findings. Yang et al. (2023), analyzing over 4.3 million patients, reported that ensemble methods such as random forest and XGBoost consistently achieved the highest predictive performance. Zhang et al. (2024) further supported these results in a meta-analysis, reporting pooled sensitivity of 0.82 and specificity of 0.91, with an overall AUC of 0.94, underscoring the robustness of ML models in clinical prediction.

The superiority of ML approaches compared to traditional sepsis scoring systems was also confirmed in more recent analyses. Yadgarov et al. (2024), through a network meta-analysis, demonstrated that neural networks and decision tree-based models outperformed clinical scales such as SOFA, NEWS, and SIRS, with pooled AUROC of 0.825. Islam et al. (2023) similarly found that ML and deep learning applied to electronic health records yielded earlier detection and improved accuracy over conventional methods, with ensemble and recurrent neural networks showing particular promise.

Despite these strengths, several limitations were consistently identified. The reviews noted heterogeneity in sepsis definitions, predictor variables, and time windows, which complicates cross-study comparisons and external validation. Fleuren et al. (2020) and Moor et al. (2021) particularly emphasized variability in model development strategies and the lack of standardized benchmarks, which hinders reproducibility. Moreover, only a minority of models had undergone external validation or prospective clinical testing, raising concerns about their generalizability to real-world settings.

Another important finding relates to the balance between model complexity and interpretability. While deep learning approaches demonstrated superior performance in some analyses (e.g., Yadgarov et al., 2024), their “black-box” nature poses challenges for clinical trust and adoption. In contrast, tree-based and logistic regression models, though sometimes slightly less accurate, offered greater transparency and easier integration into decision-support systems (Yang et al., 2023; Islam et al., 2023).

In terms of clinical implications, the integration of ML algorithms holds promise for shortening recognition times and enabling timely interventions. As highlighted by Yang et al. (2023), real-time models have the potential to identify high-risk patients several hours

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before overt clinical deterioration. This aligns with the concept of the “golden hour” in sepsis management, where earlier recognition directly improves survival outcomes. However, both Moor et al. (2021) and Islam et al. (2023) caution that without standardized reporting and large-scale validation, premature implementation could risk over-alerting clinicians and contributing to alarm fatigue. The reviewed evidence underscores the need for future research focusing on three areas: (1) standardization of sepsis definitions, predictor sets, and validation protocols across studies; (2) external, multicenter validation to ensure model robustness across diverse patient populations; and (3) clinical trials assessing the real-world impact of ML-based decision support on outcomes such as mortality, ICU length of stay, and antibiotic stewardship.

CONCLUSION

This systematic review demonstrates that artificial intelligence and machine learning models incorporating laboratory markers such as ESR and CRP, along with other routinely collected clinical data, can improve the early prediction and diagnosis of sepsis. Across diverse populations and clinical settings, these models consistently outperformed traditional scoring systems and single biomarker approaches, achieving higher sensitivity, specificity, and overall diagnostic accuracy. The evidence suggests that AI-driven tools hold particular promise for enhancing timely recognition of sepsis in adult populations, though their performance in neonatal and pediatric groups remains less reliable.

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